

Amendments to the Specification:

The paragraph starting at page 4, line 29 has been amended as follows:

In one embodiment, this invention provides isolated nucleic acid comprising DNA having at least about 800 nucleotides and at least about a 70% sequence identity to (a) a DNA molecule encoding a human clone 65 polypeptide comprising the sequence of amino acids 1 to 258 of ~~Figures 5A and 5B~~5A-5D (SEQ ID NO:3), or (b) the complement of the DNA molecule of (a). Preferably, this nucleic acid has at least one clone 65 or 320 biological activity.

The paragraph starting at page 4, line 35 has been amended as follows:

In another aspect, the invention provides isolated nucleic acid comprising DNA having at least about 700 nucleotides and at least about a 95% sequence identity to (a) a DNA molecule encoding a human clone 65 polypeptide comprising the sequence of amino acids 1 to 258 of ~~Figures 5A and 5B~~5A-5D (SEQ ID NO:3), or (b) the complement of the DNA molecule of (a). Preferably, this nucleic acid comprises DNA encoding a human clone 65 polypeptide having amino acid residues 1 to 258 of ~~Figures 5A and 5B~~5A-5D (SEQ ID NO:3), or the complement thereof.

The paragraph starting at page 6, line 14 has been amended as follows:

Also provided is a polypeptide produced by (i) hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a human clone 65 polypeptide comprising the sequence of amino acids 1 to 258 of ~~Figures 5A and 5B~~5A-5D (SEQ ID NO:3), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about a 70% sequence identity to (a) or (b), (ii) culturing a host cell comprising the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the polypeptide from the cell culture.

The paragraph starting at page 10, line 12 has been amended as follows:

~~Figures 5A and 5B~~5A-D show the derived amino acid sequence of a native-sequence human clone 65 protein from amino acids 1 to 258 (SEQ ID NO:3) and the consensus nucleotide sequence (and complementary sequence) encoding the protein (SEQ ID NOS:1 and 2, respectively), which is derived from three human clones from a human fetal liver library. There

are 2955 bp of 3' untranslated region and 777 bp of coding region in the sequence. Potential N-glycosylation sites are from amino acids 85 through 88, amino acids 138 through 141, and amino acids 245 through 248. Potential protein kinase C phosphorylation sites are at amino acids 140 through 142 and 207 through 209. Potential casein kinase II phosphorylation sites are at amino acids 81 through 84, 119 through 122, 161 through 164, and 199 through 202. Potential N-myristoylation sites are at amino acids 26 through 31, 43 through 48, and 222 through 227. A potential ATP/GTP-binding site motif A (P-loop) is at amino acids 56 through 63.

The paragraph starting at page 12, line 11 has been amended as follows:

A "native-sequence clone 65 polypeptide" comprises a polypeptide having the same amino acid sequence as a clone 65 polypeptide derived from nature. Such native-sequence clone 65 polypeptides can be isolated from nature or can be produced by recombinant or synthetic means. The term "native-sequence clone 65 polypeptide" specifically encompasses naturally-occurring truncated or other forms of a clone 65 polypeptide disclosed herein, naturally-occurring variant forms (*e.g.*, alternatively-spliced forms or splice variants), and naturally-occurring allelic variants of a clone 65 polypeptide. In one embodiment of the invention, the native-sequence clone 65 polypeptide is a full-length, native-sequence human clone 65 polypeptide comprising amino acids 1 to 258 of Figures ~~5A and 5B~~5A-5D (SEQ ID NO:3), with or without the N-terminal methionine. In another embodiment of the invention, the native-sequence clone 65 polypeptide is a full-length native-sequence mouse clone 65 polypeptide comprising amino acids 1 to 261 of Figures 1A and 1B (SEQ ID NO:6), with or without the N-terminal methionine.

The paragraph starting at page 13, line 16 has been amended as follows:

The term "clone 65 variant" means an active clone 65 polypeptide as defined below having at least about 80%, preferably at least about 85%, more preferably at least about 90%, most preferably at least about 95% amino acid sequence identity with human clone 65 having the deduced amino acid sequence shown in Figs. ~~5A and 5B~~5A-5D (SEQ ID NO:3) and/or with mouse clone 65 having the deduced amino acid sequence shown in Figs. 1A and 1B (SEQ ID NO:6). Such variants include, for instance, clone 65 polypeptides wherein one or more amino acid residues are added to, or deleted from, the N- or C-terminus of the full-length sequences of

Figures 5A-B and 1A-B (SEQ ID NOS:3 and 6, respectively), including variants from other species, but excludes a native-sequence clone 65 polypeptide.

The paragraph starting at page 17, line 14 has been amended as follows:

Alternatively, using the murine nucleotide sequences shown in Figures 1-4 (SEQ ID NOS:4, 7, 8, or 9, respectively), or the murine amino acid sequence shown in Figure 1 (SEQ ID NO:6) or the human nucleotide and amino acid sequences shown in Figures ~~5A-5B~~5A-5D (SEQ ID NOS:1 and 3), variants of native clone 65 or clone 320 are made that act as antagonists.

The paragraph starting at page 56, line 28 has been amended as follows:

The nucleotide sequence of a consensus sequence made up of all three clones (SEQ ID NO:7) is shown in Figs. 4A and 4B. The nucleotide sequence of another clone of mouse clone 320 is shown in Figs. ~~5A and 5B~~5A-5D (SEQ ID NO:8) and of yet another clone is shown in Figure 6 (SEQ ID NO:9). The consensus sequence is a mouse clone 320 sequence of 2822 bp having no obvious or apparent open reading frame, and is probably a partial clone. When RNA from tumors arising in mice in a colony established from two Wnt-1 male transgenic mice (provided by Harold Varmus at NCI) was subjected to RT-PCR using the above primers, clone 320 was strongly induced. A small section of only about 200 bp of the consensus sequence matches a region in the 3'UTR of human Wnt-5A.

The paragraph at page 57, line 12 has been amended as follows:

Four clones were identified: 65.1, 65.4, 65.5, and 65.6. The inserts to these clones were subcloned into pBluescriptTM IISK+ and its DNA sequence determined by dideoxy DNA sequencing on both strands. A consensus sequence from these clones was obtained to give both the nucleotide sequence and putative amino acid sequence for human clone 65. The consensus sequence and the derived amino acid sequence are shown in Figures ~~5A and 5B~~5A-D (SEQ ID NOS:1 and 3, respectively). Clone 65.1 (SEQ ID NO:46) starts at nucleotide position 51 and ends at 227 of SEQ ID NO:1. The second clone 65.4 (SEQ ID NO:47) starts at nucleotide position 51 and ends at 824 of SEQ ID NO:1. The third clone 65.6 (SEQ ID NO:48) starts at nucleotide position 480 and ends at 1319 of SEQ ID NO:1) in Figs. 5A-5B. This consensus sequence of Figs. 5A-5B (SEQ ID NO:1) is 93% homologous to the mouse clone 65 nucleotide

sequence of Fig. 1 (SEQ ID NO:4). See Fig. 6. By homology searching, human clone 65, like mouse clone 65, is found to be a member of the Rho, Rac, and CDC42 family. Because of the homology to the Rho and Rac family, these proteins are believed to be involved in the upregulation of cancer genes.

The paragraph starting at page 61, line 1 has been amended as follows:

DNA comprising the coding sequence of full-length human clone 65 (as shown in Figures ~~5A and 5B~~ 5A-5D, SEQ ID NO:3), or of mouse clone 65 (as shown in Figures 1A and 1B, SEQ ID NO:6), or of full-length mouse clone 320 (the partial sequences shown in Figures 2, 3, and 4; SEQ ID NOS:7, 8, and 9, respectively) is employed as a probe to screen for homologous DNAs (such as those encoding naturally- occurring variants of these particular clone 65 and 320 polypeptides in human tissue cDNA libraries or human tissue genomic libraries.